

REMARKS

Claims 1-19 are pending. Claims 13-19 are withdrawn from consideration. Claims 1-12 are rejected. Amendment to claims 8 and 9 has been made solely to overcome indefiniteness rejections and to put the claims into acceptable U.S. form. No new matter has been added. Reconsideration is requested.

Rejection under 35 USC §112, second paragraph

Claims 9 and 10 were rejected under 35 USC § 112, second paragraph, as being indefinite. Claim 9 has been amended to replace the term "the" with "a". Claim 8 has been amended to recite "foreign DNA", thereby providing antecedent basis for the recitation of this term in Claim 10. It is believed that the claims are free of indefiniteness rejections. Reconsideration and withdrawal thereof are respectfully requested.

Rejection under 35 USC §103

Claims 1-12 were rejected under 35 USC §103(a) as being unpatentable over Ilan et al. in view of DeMatteo et al and further in view of Bakker et al. This rejection is traversed for the following reasons.

The examiner stated: "The rejection of claims 1 – 12 under 35 U.S.C. 103(a) as being unpatentable over Ilan et al. (1996) J. Clin. Invest., Vol. 98 (11), 2640 – 2647, in view of DeMatteo et al. (1997) J. Virol., Vol. 71 (7), 5330 – 5335, and further in view of Bakker et al. (1999) J. Immunol., Vol. 162, 3456 – 3462, is maintained," and further stated: "Applicant's amendments to the claims and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below. "

Further, the examiner stated: "In the instant case, the rejection of record is based on the **combined** teachings of Ilan et al. in view of DeMatteo et al. and Bakker et al. The office recognizes that each reference individually does not render the instant invention obvious, however, the office has established that the combined teachings of Ilan et al., DeMatteo et al.,

and Bakker et al. render the instant invention obvious.”

Applicants respectfully submit that the position of the examiner described above is improper because it has been made on the basis of misunderstanding about the difference between the present invention and the teachings in the cited references, and a misunderstanding of the applicant's remarks responding to the previous office action. Briefly, the applicant has described the technical content of the present invention in detail in the Remarks section of the previous office action, and specifically described the technical content disclosed by the three cited references, Ilan et al., DeMatteo et al., and Bakker et al. Applicant's remarks explained in detail why there is no reasonable grounds to combine these references, and that the present invention is not taught even if these references are combined.

In response to the applicant's remarks, the examiner has stated in the present office action: “the office has established that the combined teachings of Ilan et al., DeMatteo et al., and Bakker et al. render the instant invention obvious.” However, this position is not based on the disclosure of the cited references and is therefore incorrect. The applicant again specifically describes that the present invention is never taught by the combination of the cited references.

1) First, the examiner asserts that ‘the combined teachings of Ilan et al., DeMatteo et al., and Bakker et al.’ render the instant invention obvious. However, there is no description or suggestion in any of the cited references, Ilan et al., DeMatteo et al., and Bakker et al., about the basic technical feature of the present invention, that is, “to acquire natural immunological tolerance with the use of ‘immature T lymphocyte.’” Therefore, it is obvious that the present invention is not taught by any combination of the cited references, Ilan et al., DeMatteo et al., and Bakker et al. Because there is no description of the feature in any of the cited references, no combination of the cited references can render the technical feature of the present invention obvious.

The examiner has cited Ilan et al., and stated: “Ilan et al. was cited for establishing that cells containing and expressing foreign DNA can be used to induce tolerance against the foreign

gene by directly administering the cells to the thymus,” and exemplified the disclosure of Ilan et al., “cells containing and expressing foreign DNA are directly administered to the thymus,” as a disclosure which teaches the present invention.

However, this conclusion is not correct. Briefly, in the present invention, “acquired immunological tolerance can be induced by using the above mechanism of acquiring immunological tolerance in the process of differentiation of the ‘immature T lymphocytes’ in thymus, by integrating genes expressing antigen into the ‘immature T lymphocytes’ and introducing the ‘immature T lymphocytes’ into thymus.” By a method such as Ilan's, wherein only “cells containing and expressing foreign DNA” are administered, and “immature T lymphocytes” are not used, the advantage of the present invention, that is, that “acquired immunological tolerance can be induced by using the above mechanism of acquiring immunological tolerance in the process of differentiation of the ‘immature T lymphocytes’ in thymus,” cannot be obtained. As stated above, Ilan et al. does not disclose “inducing acquired immunological tolerance by introducing ‘immature’ cells,” therefore, even if this cited reference and the description of other cited references such as Bakker et al. are combined, the present invention is not taught by the combination.

2) The examiner has stated: “Bakker et al. was then cited to further supplement Ilan et al. and DeMatteo et al. by teaching methods of infecting fetal T lymphocytes with recombinant adenovirus in vitro in fetal thymic organ culture,” and further stated: “motivation to substitute fetal T lymphocytes for hepatocytes in the methods of Ilan et al. is provided by all of Ilan et al., DeMatteo et al., and Bakker et al.” This conclusion of the examiner is also improper. In this regard, the examiner has stated that “The teachings of Ilan et al. were supplemented with the teachings of DeMatteo et al., and Bakker et al. Specifically, DeMatteo et al. was cited to supplement the teaching of Ilan et al., by teaching that adenovirus is capable of infecting fetal T lymphocytes in fetal thymus and further that the transduced fetal T lymphocytes induce tolerance (DeMatteo et al., page 5330, abstract, and Figure 1).” However, as DeMatteo et al. does not

describe “fetal thymus,” this conclusion of the examiner is not correct.

The applicant rebuts the examiner’s statement, “motivation to substitute fetal T lymphocytes for hepatocytes in the methods of Ilan et al. is provided by Bakker et al.,” as follows.

As described in the cited reference, Bakker et al. discloses use of a novel technique combining “adenovirus-mediated gene transfer” and “fetal thymic organ culture (FTOC)” “to determine at which stage of fetal thymic development NF- κ B is critical” (for example, see abstract, page 3456, 10th to 7th lines from the bottom). In other words, this reference discloses that adenovirus-mediated introduction is employed when a gene is introduced into “fetal thymic organ culture”, and this gene introduction by Bakker et al. is the same method as that of Ilan et al., wherein adenoviral vectors are used to introduce foreign DNA into thymus. Therefore, even when Ilan et al. and Bakker et al. are combined, the combination only teaches that adenoviral vectors are used to introduce foreign DNA into thymus. The examiner has stated: “motivation to substitute fetal T lymphocytes for hepatocytes” is provided by Bakker et al. However, as Bakker et al. does not disclose that gene-transferred cells are further used for gene transfer, the examiner’s position is groundless. Further, as previously mentioned, Ilan et al. and Bakker et al. do not disclose “acquired immunological tolerance can be induced by introducing ‘immature’ cells”. Therefore, it is clear that even if the cited references Ilan et al. and Bakker et al. are combined, the present invention is not taught by the combination.

3) As specifically described above, it is respectfully submitted that the position of the examiner, who has stated: “the office has established that the combined teachings of Ilan et al., DeMatteo et al., and Bakker et al. render the instant invention obvious”, is groundless once the disclosures of the cited references are correctly understood. Reconsideration and withdrawal of the rejection are respectfully requested.

Applicants: Yousuke TAKAHAMA et al.
Appl. No.: 09/889,321


CONCLUSION

As stated above, even when the disclosures of Bakker et al., DeMatteo et al., and Ilan et al., are considered together, the present invention is not taught by the combination. Therefore, it is respectfully requested that the rejection of claims 1-12 under 35 U.S.C.103 (a) as being unpatentable over Ilan et al. (1996), in view of DeMatteo et al. (1997), and further in view of Bakker et al. (1999) be withdrawn.

All rejections having been addressed, it is respectfully submitted that the application is in order for allowance, and Notice to that effect is respectfully requested.

Respectfully submitted,

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Ann S. Hobbs, Ph.D.
Registration No. 36,830
VENABLE
P.O. Box 34385
Washington, D.C. 20043-9998
Telephone: (202) 344-4000